Claims

1. A glycosylated or nonglycosylated proteinaceous compound having agonist activity for at least one glycoprotein hormone

$$\beta^{1}$$
-(linker¹)_n1- β^{2} -(linker²)_n2- β^{3} -(linker³)_n3- α

$$\beta^1$$
-(linker¹)_n1- β^2 -(linker²)_n2- α -(linker³)_n3- β^3

$$\beta^1\text{-}(linker^1)_{n^1}\text{-}\alpha\text{-}(linker^2)_{n^2}\text{-}\beta^2\text{-}(linker^3)_{n^3}\text{-}\beta^3$$

$$\alpha$$
-(linker¹)_n1- β 1-(linker²)_n2- β 2-(linker³)_n3- β 3

wherein α is the α subunit of a vertebrate glycoprotein hormone or a variant thereof;

10

20

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each β is independently a glycoprotein β subunit or a variant thereof; each "linker" is a hydrophilic, flexible spacer equivalent to a peptide containing 1-100 amino acid residues; and

each n is a 0 or 1;

said compound optionally comprising one or more additional β^x (linker^x)_nx and/or one or more additional α subunits.

2. The compound of claim 1 which is of the formula

(1)
$$\beta^1$$
-(linker¹)_n1- β^2 -(linker²)_n2- β^3 -(linker³)_n3- α

(2)
$$\beta^{1}$$
-(linker¹)_n¹- β^{2} -(linker²)_n²- α -(linker³)_n³- β^{3} ;

(3)
$$\beta^1$$
-(linker¹)_n1-\alpha-(linker²)_n2-\beta^2-(linker³)_n3-\beta^3

(4)
$$\alpha$$
-(linker¹)_n1- β 1-(linker²)_n2- β 2-(linker³)_n3- β 3

(5)
$$\beta^1(\text{linker}^1)_{n^2} - \beta^2(\text{linker}^2)_{n^2} - \beta^3(\text{linker}^3)_{n^3} - \beta^4(\text{linker}^4)_{n^4} - \alpha;$$

(6)
$$\beta^1 (linker^1)_{n^1} - \beta^2 (linker^2)_{n^2} - \beta^3 (linker^3)_{n^3} - \alpha - \beta^4 (linker^4)_{n^4};$$

(7)
$$\beta^1(\text{linker}^1)_{n^1} - \beta^2(\text{linker}^2)_{n^2} - \alpha - \beta^3(\text{linker}^3)_{n^3} - \beta^4(\text{linker}^4)_{n^4}$$
;

(8)
$$\beta^1(\text{linker}^1)_{n^1} - \alpha - \beta^2(\text{linker}^2)_{n^2} - \beta^3(\text{linker}^3)_{n^3} - \beta^4(\text{linker}^4)_{n^4}$$
; or

(9)
$$\alpha - \beta^1 (\operatorname{linker}^1)_{n^1} - \beta^2 (\operatorname{linker}^2)_{n^2} - \beta^3 (\operatorname{linker}^3)_{n^3} - \beta^4 (\operatorname{linker}^4)_{n^4}$$

25

3. The compound of claim 1 or 2 wherein each β is different.

15

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- 4. The compound of claim 1 or 2 wherein at least one linker is independently a complete or partial CTP comprising at least one glycosylation site or a variant thereof, wherein CTP refers to the amino acid sequence at positions 112-118 to 145 of human chorionic gonadotropin β subunit.
 - 5. The compound of claim 1 or 2 which is a protein.
- 6. The compound of claim 1 or 2 wherein said protein consists of naturally occurring amino acids.
- 7. The compound of claim 1 or 2 wherein each β and α subunit is human native subunit.
 - 8. The compound of claim 1 which is of formula (1).
 - 9. The compound of claim 8 which is TSH β -CTP-FSH β -CTP-CG β - α .
 - 10. The compound of claim 2 which is of formula (5).
 - 11. The compound of claim 10 wherein each β subunit is different.
- 12. A pharmaceutical composition which comprises the compound of claim 1 or 2 in admixture with a suitable pharmaceutical excipient.
 - 13. The compound of claim 1 or 2 coupled to a solid support.
 - 14. Antibodies immunospecific for the compound of claim 1 or 2.
- 15. A DNA or RNA molecule which comprises a nucleotide sequence encoding the protein of claim 6.

5

- 16. An expression system for production of an agonist of at least one glycoprotein hormone which expression system comprises a first nucleotide sequence encoding the protein of claim 6 operably linked to control sequences for effecting the expression of said first nucleotide sequence.
- 17. The expression system of claim 16 which further contains a second nucleotide sequence encoding a signal peptide operably linked to the protein encoded by said first nucleotide sequence.
 - 18. Cells modified to contain the expression system of claim 17.
 - 19. Cells modified to contain the expression system of claim 18.
- 20. A method to produce a single-chain agonist of at least one glycoprotein hormone which method comprises culturing the cells of claim 18 under conditions wherein said protein is produced; and

recovering said protein from the culture.

21. A method to produce a single-chain agonist of at least one glycoprotein hormone which method comprises culturing the cells of claim 19 under conditions wherein said protein is produced; and

recovering said protein from the culture.